Ninetieth Advisory Committee on Animal Feedingstuffs meeting
3rd April 2024 – Online meeting

ACAF	**FSA**
Nick Jonsson (Chair)	Nathan Allen
Martin Briggs	Mark Bond
Emily Burton	Aaron Bradshaw
Katrina Campbell	Emily Davies
Matthew Fisher	Edward Fuller
Hannah Kane	Beth Hall
Oonagh Markey	Emily Hudson
Susan MacDonald	Michelle Hutchinson
Chris McAlinden	David Kovacic
Donald Morrison	Kaila Lee
Derek Renshaw	Francisco Matilla
Mike Salter	Barry Maycock
Adam Smith	James Metcalfe
Christel Wake	Chris Rundle
Helen Warren	Lucy Smythe
Nick Wheelhouse	Shila Sultana
	Johann Trotter

1. Apologies

No apologies were received.

2. Welcome

The Chair welcomed members of the Committee, Secretariat and observers from the Devolved Administrations.

3. Risk Assessment update

The Regulated Products Team Leader Francisco Matilla-Garcia updated the Committee, highlighting that an additional 10 Safety Assessments have been published, four of which were ACAF-led and six progressed through the ORO route. There are currently 57 applications within the risk assessment process, with another 75 awaiting validation. 24 applications are in the process of being assessed by ACAF and 10 awaiting evaluation by the Committee. An update was provided regarding potential changes that may arise moving forward in terms of allocation of applications to ACAF or the two other risk assessment processes. Two new members were also welcomed to the Secretariat. Additionally, a new organisational chart outlining the risk assessment team was signposted to the Committee, as well as the SAC activities summary.

4. Policy Update

Feed Additives Senior Policy Advisor, Mark Bond, briefed the Committee on the number of feed additive applications currently in the system and the number of new applications received since the last meeting. An update regarding the current recruitment campaign was provided, as well as an update on the third set of feed additives going to consultation for authorisation. Members were also notified of the recent publication of the consultation on the reform of Regulated Products.

5. Minutes from 89th Meeting

The Committee reviewed the minutes from the 89th ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Dossier for assessment: RP1421 HiPhorius (6-phytase)

Adam Smith declared a direct conflict of interest and left the meeting for this item.

An application was evaluated for the additive HiPhorius. The applicant requested the authorisation of the additive for use in poultry, swine, and aquaculture. The additive falls under the category of "zootechnical additive" and functional group "digestibility enhancer".

B. cereus testing was previously requested however the Committee discussed the guidance and agreed that unless products are produced by bacteria from the taxonomic class Bacilli (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?mode=Tree&id=91061&lvl=3&lin=f&keep=1&srchmode=1&unlock) which includes genera commonly used in feed additives (e.g. *Bacillus* spp., *Lactobacillus spp*., *Pediococcus spp*., *Streptococcus spp*., *Lactococcus spp*., *Enterococcus spp*,) testing for *B. cereus* will not be requested. For the manufacturing process, the Committee noted that a carbohydrate binder was referenced but remained unclear as to its composition. **The applicant would be asked to clarify the composition of the carbohydrate binder.** The provided MSDS were not in English and did not directly relate to the materials in the lists of ingredients. **The applicant would be asked to provide translated MSDS documents for the appropriate list of ingredients.** It was also noted that no HACPP details, control points, or assurance certificates of the supplying organisation or the manufacturing plant were provided. **The applicant would be asked to provide information on HACCP, including critical control plants, and the relevant assurance certificates.** The Committee agreed that the solid formulations were essentially non-dusty and did not contain particles small enough to deposit in the lungs of exposed workers. Members noted that for the pelleted feed trial, no retention time was given. **The applicant would be asked to provide the retention time used in this study.**

The applicant utilised a NOAEL from a rat sub chronic study instead of submitting tolerance studies. The Committee agreed that an acceptable margin of safety was

demonstrated for the range of animals covered in the conditions of use. The Committee concluded that the additive is non-genotoxic based on the two studies provided: a bacterial reverse mutation assay and an in vitro micronucleus test. Based on these genotoxicity studies and sub chronic oral toxicity studies, no reason for concern was raised regarding consumer safety. The Committee agreed that the additive has the potential to be a respiratory sensitiser, as do all other enzyme products. In the absence of tests for skin sensitisation, the additive was also regarded as a potential skin sensitiser. Within Annex 3.3.3, a material is referred to as 'X-phos, batch ELN-20-THF-004', **the applicant would be asked to clarify the identity of this material**. The Committee noted that SDS documentation for HiPhorius 40 and 50 L specify P3 respiratory whereas 10 and 20 L only state 'approved filter'. **The applicant would be asked to clarify these discrepancies.** No concerns were raised by the Committee regarding safety for the environment as the enzyme is extensively metabolised.

The Committee concluded that the additive is efficacious in growing birds however further discussion would be held offline to determine whether two of the provided studies could be considered within the application, due to experimental issues. The increased copper levels within one of the efficacy studies was discussed with the Committee agreeing that copper levels should have little to no impact on additive efficacy and that from a scientific perspective efficacy has been demonstrated. ACAF however requested a report from Policy regarding the legal status of the studies and their eligibility for consideration.

7. Dossier for assessment: RP1280 Formaldehyde

No conflicts of interest were declared for this item.

Members decided to postpone discussion of this application until further information has been provided by the applicant relating to the identity of the additive to be authorised.

8. Dossier for assessment: RP1579 *Pediococcus acidilactici* CNCM I-4622

No conflicts of interest were declared for this item.

An application was evaluated for *Pediococcus acidilactici* CNCM I-4622. The applicant requested a new authorisation of the additive for all insect species and categories. The additive falls under the category "zootechnical additives" and functional group "physiological condition stabilisers". The Committee carried out a partial risk assessment on the efficacy section of the application.

Members discussed the rationale for only evaluating the efficacy section of this application. They were satisfied with the rationale that the additive was assessed previously (RP29) and was concluded to be safe for the target species, consumers, and the environment.

Prior to the meeting, members reviewed a document prepared by specialist Maureen Wakefield, addressing efficacy. Members discussed several points outlined in this document, noting that no details of a quantitative or qualitative assessment of the source colonies were provided, therefore the health status of the colonies used cannot be assessed. They also indicated that as one single parameter was used to assess efficacy, a greater range of biological and behavioural parameters should have been measured and the addition of the additive at a colony level under field conditions should have been assessed. Members also noted that the applicant has applied for use in all insects, however the study provided only looked at efficacy for a single species and single microsporidian pathogen and therefore effects on other biological stressors cannot be assumed. Insect gut environments can also differ depending on diet; therefore evidence would be needed for a broader range of insects. Members concluded that insufficient evidence has been provided to allow for extrapolation to all insect species and categories, therefore, **members could not conclude positively on the efficacy of this additive.**

9. RP1335 Bio D 1.25% 25-hydroxycholecalciferol

Mike Salter and Emily Burton declared an interest, which was deemed to not pose a conflict, and remained in the meeting for the discussion.

An application was submitted for 1.25% 25-hydroxycholecalciferol, a 25-hydroxy analogue of vitamin D3, seeking authorisation for use in poultry for fattening, poultry for laying, and pigs. An additive with the same active ingredient is already authorised for use in poultry, pigs and all ruminants, however this additive is produced by the non-QPS organism, *Pseudonocardia autotrophica*, therefore a new safety assessment was necessary.

The Secretariat noted that the safety studies provided were performed using an additive produced by a different strain to that under assessment (i.e., *P. autotrophica* 10M213 vs. M301). The applicant had provided insufficient evidence to demonstrate the toxicological bioequivalence of the strain under assessment and the strain used in the safety studies. Therefore, **this application will not be considered for full risk assessment by ACAF at this stage.**

10. Response to RFI: RP1072 Avatec 150 G

No conflicts of interest were declared for this item.

Members reviewed the updated bioinformatic analysis provided, concluding that it adequately addressed the Committee's queries. The HACCP and quality assurance documentation provided was deemed suitable for assessment, however, documentation for the American production site had not been provided. **The applicant would be asked to provide HACCP and quality assurance documentation for the American production site.** The documentation provided for pelleting stability did not contain the conditioning time for the process. **The applicant would be asked to provide the conditioning time for the process and reminded**

that in the absence of data the Committee will be unable to conclude on pelleting stability.

11. Response to RFI: RP1137 CanBiocin

No conflicts of interest were declared for this item.

The Committee were satisfied with the *Salmonella* and *B. cereus* testing data provided by the applicant. The Committee discussed the manufacturers' data sheets and SDS documentation for glycerol, CB1 and sodium acetate anhydrous. The MSDS provided for glycerine and sodium acetate were over 5 years old and as such **the applicant would be asked to provide more recent MSDS documentation.** The Committee were satisfied that it is unlikely that the additive would contain any undesirable carry over of culture media. However, no analysis of arsenic was provided, therefore **the applicant would be asked to provide arsenic testing for the additive.** The applicant's response explaining the clumping of *L. casei* was found to be unsatisfactory. As the applicant stated that the clumping of *L. casei* has been resolved in recent batches, **the applicant would be asked to provide testing of additional batches to confirm this.**

The Committee discussed the applicant's decision to substitute the *E. faecium* WF-3 strain in the additive with *E. faecium* PCEF02 to overcome the mobile genetic element identified within the original strain. The ACAF concluded that **due to the substitution of the strain, the whole dossier should be resubmitted with new efficacy and safety trials on the appropriate strain**. The Committee also noted that the submitted stability studies were undertaken using the original strain and as such **the stability studies would need to be performed again using the *E. faecium* strain PCEF02**.

12. Response to RFI: RP1243 L-methionine (*C. glutamicum* & *E.coli*)

No conflicts of interest were declared for this item.

Members noted that testing for *Bacillus cereus* had been provided and that the results were within the limits described in EFSA guidance. The applicant provided MSDS documentation for the ingredients used in the manufacturing process, however, one of the documents was lacking in detail and deemed unsuitable for assessment. **The applicant would be asked to provide an updated version of this MSDS document.** The updated manufacturing process document did not provide sufficient detail, with the critical points of the process not included. The HACCP documentation was redacted and therefore could not be assessed. **The applicant would be asked to provide an updated flow chart for the manufacturing process ensuring the critical control points of the process are clearly indicated. The applicant would also be asked to provide an un-redacted HACCP documentation for assessment.**

Owing to the proposed conditions of use of the additive in all species, members concluded that a stability trial in a further form of feed would be required to allow a comprehensive assessment of stability in line with EFSA guidance. **The applicant would be asked to provide a stability study in a further form of feed.** The data provided for pelleting stability did not include the conditioning time and therefore could not be assessed. **The applicant would be asked to provide the conditioning time for the pelleting process.** The applicant re-submitted the label, stating that this version is the highest quality available. This would be reviewed by members offline prior to issuing a request for information to the applicant. **The applicant would be reminded that in the absence of the requested data the Committee would be unable to conclude on certain areas of the dossier.**

13. Response to RFI: RP1282 *Levilactobacillus brevis* DSMZ 21982

Helen Warren declared an indirect conflict of interest and remained in the meeting for the discussion.

Members were satisfied with the response from the applicant regarding testing for *Bacillus cereus*, batch to batch variation of the active agent in a total of five batches, PFGE analysis to evaluate the genetic stability of the bacterial strain, and the temperatures at which the stability of the additive in water was tested.

Regarding dusting potential, the applicant stated that all Microferm bacteria are prepared in the same way, therefore dusting potential data from one bacterial strain can be applied to other bacterial strains. Members stated that data of a different bacteria strain is not a suitable substitute for data on the formulated additive product in this application. Therefore, the additive is assumed to be very dusty with the potential to cause respiratory sensitisation in exposed workers and suitable measures will need to be taken to protect workers from inhalation exposure.

The sample label provided by the applicant was evaluated. It was noted that it did not reference the stability of the additive in water, however there was a statement in the application to ‘use within 3 days of mixing’. **The applicant is asked to update the label taking this into consideration**. The applicant provided several MSDSs for ingredients, **however the applicant is asked to provide an updated MSDS for milk-based products, which includes a date**. Members were satisfied with the HACCP plan provided by the applicant. The applicant stated “Microferm Ltd acts as “gatekeeper” which “the FAMI-QS auditors are aware of”. **The applicant is asked to provide this audit report that has been referred to**.

As this application is for a renewal, it has now been placed under active case management.

14. Response to RFI: RP1298 Ronozyme HiPhos

Adam Smith declared a direct conflict of interest and left the meeting for this item.

Upon request by the ACAF, the applicant provided 24-month stability data for the additive over 3 batches. The Committee noted that the decline in average residual activity over the 24 months is compensated by necessary overfill of the additive. **The applicant would be asked to provide the overage data currently supplied and if they can predict future overages with the new production strain.** The Committee were satisfied with the *B. cereus*, yeast and filamentous fungi testing data provided by the applicant. However, **the applicant would be asked to provide accreditation for the laboratory that conducted the testing and the test methods utilised**. The applicant was asked to provide data showing the differences between DSMZ 22594 strain and the DMSZ 33699 strain and to describe any variation. The applicant provided DNA alignment of the phytase gene of the two strains. **Therefore, the applicant would be asked to provide phylogenetic analysis and characterization of the two strains**.

15. Response to RFI: RP1341 Avizyme 1505

No conflicts of interest were declared for this item.

The Committee reviewed the updated bioinformatics data and noted that the strain used in the absence of viable production strain studies was unclear. **The applicant would be asked to clarify the strain used in these studies.** Members were unable to conclude on the presence of AMR genes in the final product from the updated information provided. **The applicant would be asked to provide further information to demonstrate the absence of the AMR genes from the final product.** The data provided for the primer selection would be reviewed offline prior to an RFI being issued to the applicant. The Committee reviewed the updated information for the manufacturing process and concluded that the updated flow chart and FAMI-QS documentation were suitable for assessment. Several of the MSDS documents provided were not appropriate for assessment, **the applicant would be asked to review the MSDS documentation and ensure all documents provided have been reviewed within the past five years.** Members noted that studies for skin sensitisation had not been provide by the applicant. **The applicant would be asked to provide studies for skin sensitisation and reminded in the absence of data the additive would be regarded as a potential skin sensitiser.**

16. Response to RFI: RP1512 PB6 (*Bacillus velezensis* ATCC PTA-6737)

No conflicts of interest were declared for this item.

More recent analytical data demonstrating batch-to-batch variation was provided, as well as for impurity testing. The Committee were satisfied with this data, however **the applicant would be asked to provide testing for *Bacillus cereus*.** Although additional documentation regarding the laboratories used was provided, **the applicant would be asked to confirm what recognised assurance the GeneFerm laboratory holds that demonstrates compliance with international standards for testing and calibration laboratories**. Additionally, **the applicant**

would be asked to provide details of the critical control points for the GeneFerm manufacturing process. HACCP documentation has not been provided for Kemin Industries, therefore **the applicant would be asked to provide this documentation, including critical control points**. As requested, updated MSDS have been provided for the ingredients used in the production process, however one of the MSDS was from 2015, one was not dated and the other had an English translation that was unreadable. **The applicant would be asked to provide more recent MSDS for these three ingredients that are legible and clearly dated**. A missing quality control document was provided as requested, detailing that every lot is tested for heavy metals, dioxins, pesticides, antibiotics and mycotoxins. A representative label had been provided, however the Committee had noted that the label does not give any advice to workers on the safe handling of the additive. Information regarding conditioning time should also be included. **The applicant would therefore be asked to provide an updated label taking these points into consideration.**

The applicant was asked to explain the discrepancy noted in the dusting potential values given, confirming that the dusting potential values for this additive are quite high**.**

Further clarification was requested regarding efficacy and the proposed doses for use in growing pigs and for sows and reproductive stages of minor porcine species. **The Committee assessed the information provided and concluded that the additive is efficacious in weaned piglets at a dose of 1 x 10^7 CFU/kg complete feed and has the potential to be efficacious in sows and growing pigs at a dose of 1 x 10^8 CFU/kg complete feed.**

17. Draft safety assessments: RP552, RP634, RP812, RP814, RP1015, RP1039/1040 and RP1111.

Members were presented with draft Committee's Advice documents for applications RP812, RP814, RP1039/1040 and RP1111.

The Committee was also presented with the final drafts of the Committee's Advice documents for applications RP552, RP634 and RP1015. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

18. Microbiology presentation

Due to time constraints, it was decided that the microbiology presentation prepared by several Committee members would be postponed to the next ACAF meeting.

19. Any other business

An update on upcoming applications was provided.

Next ACAF meeting: 11th June 2024 in person (London).